

Executive Summary: Guidelines for the Primary Prevention of Stroke

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of these guidelines as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons, the Congress of Neurological Surgeons, and the Preventive Cardiovascular Nurses Association

James F. Meschia, MD, FAHA, Chair; Cheryl Bushnell, MD, MHS, FAHA, Vice-Chair; Bernadette Boden-Albala, MPH, DrPH; Lynne T. Braun, PhD, CNP, FAHA; Dawn M. Bravata, MD; Seemant Chaturvedi, MD, FAHA; Mark A. Creager, MD, FAHA; Robert H. Eckel, MD, FAHA; Mitchell S.V. Elkind, MD, MS, FAAN, FAHA; Myriam Fornage, PhD, FAHA; Larry B. Goldstein, MD, FAHA; Steven M. Greenberg, MD, PhD, FAHA; Susanna E. Horvath, MD; Costantino Iadecola, MD; Edward C. Jauch, MD, MS, FAHA; Wesley S. Moore, MD, FAHA; John A. Wilson, MD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Functional Genomics and Translational Biology, and Council on Hypertension

These updated guidelines on stroke prevention appear more than 3 years since the publication of its predecessor. Recommendations follow the American Heart Association (AHA) and the American College of Cardiology methods of classifying the size and certainty of treatment effect (Tables 1 and 2). We strove for consistency with other AHA guidelines and minimized overlap with the recently published AHA guidelines for the prevention of stroke in women. Table 3 summarizes important revisions to the guidelines. It is worth noting key sections where changes have been made or considered but not made. Regarding the use of statin medications, emphasis has shifted from achieving certain target levels of serum LDL cholesterol to initiating therapy based on estimated risk of cardiovascular events. The updated guidelines recommend that people who meet or exceed certain risk thresholds should be initiated on statin therapy. The higher the estimated risk, the more intensive the statin therapy should be. CHA₂DS₂-VASc is now regarded as the preferred tool for stratification of risk for stroke for patients with atrial fibrillation, and we acknowledge the roles that dabigatran, apixaban, and rivaroxaban now play in preventing stroke in this patient population. Regarding revascularization of asymptomatic carotid stenosis, the updated guidelines adhere to precedent. However, a net

benefit of revascularization in the setting of optimal modern medical therapy is not well established. We hope the busy practitioner finds this executive summary useful, but encourage reading the full length version as time permits.

Assessing the Risk of First Stroke: Recommendations

1. The use of a risk assessment tool such as the AHA/ACC CV Risk Calculator (<http://my.americanheart.org/cvriskcalculator>) is reasonable because these tools can help identify individuals who could benefit from therapeutic interventions and who may not be treated on the basis of any single risk factor. These calculators are useful to alert clinicians and patients of possible risk, but basing treatment decisions on the results needs to be considered in the context of the overall risk profile of the patient (*Class IIa; Level of Evidence B*).

Genetic Factors: Recommendations

1. Obtaining a family history can be useful in identifying people who may have increased stroke risk (*Class IIa; Level of Evidence A*).

The full text version is available online at <http://stroke.ahajournals.org/lookup/doi/10.1161/STR.0000000000000046>.

The American Heart Association requests that the full-text version of this document be used when cited: Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, Creager MA, Eckel RH, Elkind MSV, Fornage M, Goldstein LB, Greenberg SM, Horvath SE, Iadecola C, Jauch EC, Moore WS, Wilson JA; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Functional Genomics and Translational Biology, and Council on Hypertension. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:3754–3832.

© 2014 American Heart Association, Inc.

Stroke is available at <http://stroke.ahajournals.org>

- Referral for genetic counseling may be considered for patients with rare genetic causes of stroke (*Class IIb; Level of Evidence C*).
- Treatment of Fabry disease with enzyme replacement therapy might be considered, but has not been shown to reduce the risk of stroke, and its effectiveness is unknown (*Class IIb; Level of Evidence C*).
- Noninvasive screening for unruptured intracranial aneurysms in patients with ≥ 2 first-degree relatives with SAH or intracranial aneurysms might be reasonable (*Class IIb; Level of Evidence C*).¹¹⁰
- Noninvasive screening may be considered for unruptured intracranial aneurysms in patients with autosomal-dominant polycystic kidney disease and ≥ 1 relatives with autosomal-dominant polycystic kidney disease and SAH or ≥ 1 relatives with autosomal-dominant polycystic kidney disease and intracranial aneurysm (*Class IIb; Level of Evidence C*).
- Noninvasive screening for unruptured intracranial aneurysms in patients with cervical fibromuscular dysplasia may be considered (*Class IIb; Level of Evidence C*).
- Pharmacogenetic dosing of vitamin K antagonists may be considered when therapy is initiated (*Class IIb; Level of Evidence C*).
- Noninvasive screening for unruptured intracranial aneurysms in patients with no more than 1 relative with SAH or intracranial aneurysms is not recommended (*Class III; Level of Evidence C*).
- Screening for intracranial aneurysms in every carrier of autosomal-dominant polycystic kidney disease or Ehlers-Danlos type IV mutations is not recommended (*Class III; Level of Evidence C*).
- Genetic screening of the general population for the prevention of a first stroke is not recommended (*Class III; Level of Evidence C*).
- Genetic screening to determine risk for myopathy is not recommended when initiation of statin therapy is being considered (*Class III; Level of Evidence C*).

Physical Inactivity: Recommendations

- Physical activity is recommended because it is associated with a reduction in the risk of stroke (*Class I; Level of Evidence B*).
- Healthy adults should perform at least moderate- to vigorous-intensity aerobic physical activity at least 40 min/d 3 to 4 d/wk¹²⁷ (*Class I; Level of Evidence B*).

Dyslipidemia: Recommendations

- In addition to therapeutic lifestyle changes, treatment with an HMG coenzyme-A reductase inhibitor (statin) medication is recommended for the primary prevention of ischemic stroke in patients estimated to have a high 10-year risk for cardiovascular events as recommended in the 2013 "ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults"¹⁶⁹ (*Class I; Level of Evidence A*).
- Niacin may be considered for patients with low HDL cholesterol or elevated Lp(a), but its efficacy in preventing

ischemic stroke in patients with these conditions is not established. Caution should be used with niacin because it increases the risk of myopathy (*Class IIb; Level of Evidence B*).

- Fibric acid derivatives may be considered for patients with hypertriglyceridemia, but their efficacy in preventing ischemic stroke is not established (*Class IIb; Level of Evidence C*).
- Treatment with nonstatin lipid-lowering therapies such as fibric acid derivatives, bile acid sequestrants, niacin, and ezetimibe may be considered in patients who cannot tolerate statins, but their efficacy in preventing stroke is not established (*Class IIb; Level of Evidence C*).

Diet and Nutrition: Recommendations

- Reduced intake of sodium and increased intake of potassium as indicated in the US Dietary Guidelines for Americans are recommended to lower BP (*Class I; Level of Evidence A*).
- A DASH-style diet, which emphasizes fruits, vegetables, and low-fat dairy products and reduced saturated fat, is recommended to lower BP^{127,218} (*Class I; Level of Evidence A*).
- A diet that is rich in fruits and vegetables and thereby high in potassium is beneficial and may lower the risk of stroke (*Class I; Level of Evidence B*).
- A Mediterranean diet supplemented with nuts may be considered in lowering the risk of stroke (*Class IIa; Level of Evidence B*).

Hypertension: Recommendations

- Regular BP screening and appropriate treatment of patients with hypertension, including lifestyle modification and pharmacological therapy, are recommended (*Class I; Level of Evidence A*).
- Annual screening for high BP and health-promoting lifestyle modification are recommended for patients with prehypertension (SBP of 120 to 139 mm Hg or DBP of 80 to 89 mm Hg) (*Class I; Level of Evidence A*).
- Patients who have hypertension should be treated with antihypertensive drugs to a target BP of $<140/90$ mm Hg (*Class I; Level of Evidence A*).
- Successful reduction of BP is more important in reducing stroke risk than the choice of a specific agent, and treatment should be individualized on the basis of other patient characteristics and medication tolerance (*Class I; Level of Evidence A*).
- Self-measured BP monitoring is recommended to improve BP control. (*Class I; Level of Evidence A*).

Obesity and Body Fat Distribution: Recommendations

- Among overweight (BMI=25 to 29 kg/m²) and obese (BMI >30 kg/m²) individuals, weight reduction is recommended for lowering BP (*Class I; Level of Evidence A*).

Table 1. Applying Classification of Recommendations and Level of Evidence

		SIZE OF TREATMENT EFFECT												
ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT		CLASS I <i>Benefit >>> Risk</i> Procedure/Treatment SHOULD be performed/ administered	CLASS IIa <i>Benefit >> Risk</i> <i>Additional studies with focused objectives needed</i> IT IS REASONABLE to per- form procedure/administer treatment	CLASS IIb <i>Benefit ≥ Risk</i> <i>Additional studies with broad objectives needed; additional registry data would be helpful</i> Procedure/Treatment MAY BE CONSIDERED	CLASS III <i>No Benefit</i> or CLASS III <i>Harm</i> <table><tr><th></th><th>Procedure/ Test</th><th>Treatment</th></tr><tr><td>COR III: No benefit</td><td>Not Helpful</td><td>No Proven Benefit</td></tr><tr><td>COR III: Harm</td><td>Excess Cost w/o Benefit or Harmful</td><td>Harmful to Patients</td></tr></table>		Procedure/ Test	Treatment	COR III: No benefit	Not Helpful	No Proven Benefit	COR III: Harm	Excess Cost w/o Benefit or Harmful	Harmful to Patients
		Procedure/ Test	Treatment											
	COR III: No benefit	Not Helpful	No Proven Benefit											
	COR III: Harm	Excess Cost w/o Benefit or Harmful	Harmful to Patients											
	LEVEL A Multiple populations evaluated*	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses									
LEVEL B Limited populations evaluated*	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies										
LEVEL C Very limited populations evaluated*	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care										
Suggested phrases for writing recommendations		should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated should not be performed/ administered/ other is not useful/ beneficial/ effective	COR III: Harm potentially harmful causes harm associated with excess morbid- ity/mortality should not be performed/ administered/ other								
Comparative effectiveness phrases†		treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B											

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

2. Among overweight (BMI=25 to 29 kg/m²) and obese (BMI >30 kg/m²) individuals, weight reduction is recommended for reducing the risk of stroke (*Class I; Level of Evidence B*).

Diabetes: Recommendations

1. Control of BP in accordance with an AHA/ACC/CDC Advisory²¹⁸ to a target of <140/90 mmHg is recommended in patients with type 1 or type 2 diabetes mellitus (*Class I; Level of Evidence A*).
2. Treatment of adults with diabetes mellitus with a statin, especially those with additional risk factors, is

recommended to lower the risk of first stroke (*Class I; Level of Evidence A*).

3. The usefulness of aspirin for primary stroke prevention for patients with diabetes mellitus but low 10-year risk of CVD is unclear (*Class IIb; Level of Evidence B*).
4. Adding a fibrate to a statin in people with diabetes mellitus is not useful for decreasing stroke risk (*Class III; Level of Evidence B*).

Cigarette Smoking: Recommendations

1. Counseling, in combination with drug therapy using nicotine replacement, bupropion, or varenicline, is

Table 2. Definition of Classes and Levels of Evidence Used in AHA/ASA Recommendations

Class I	Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective.
Class II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa	The weight of evidence or opinion is in favor of the procedure or treatment.
Class IIb	Usefulness/efficacy is less well established by evidence or opinion.
Class III	Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful.
Therapeutic recommendations	
Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses
Level of Evidence B	Data derived from a single randomized trial or nonrandomized studies
Level of Evidence C	Consensus opinion of experts, case studies, or standard of care
Diagnostic recommendations	
Level of Evidence A	Data derived from multiple prospective cohort studies using a reference standard applied by a masked evaluator
Level of Evidence B	Data derived from a single grade A study or one or more case-control studies, or studies using a reference standard applied by an unmasked evaluator
Level of Evidence C	Consensus opinion of experts

AHA/ASA indicates American Heart Association/American Stroke Association

recommended for active smokers to assist in quitting smoking (*Class I; Level of Evidence A*).

2. Abstinence from cigarette smoking is recommended for patients who have never smoked on the basis of epidemiological studies showing a consistent and overwhelming relationship between smoking and both ischemic stroke and SAH (*Class I; Level of Evidence B*).
3. Community-wide or statewide bans on smoking in public spaces are reasonable for reducing the risk of stroke and MI (*Class IIa; Level of Evidence B*).

AF: Recommendations

1. For patients with valvular AF at high risk for stroke, defined as a CHA₂DS₂-VASC score of ≥ 2 and acceptably low risk for hemorrhagic complications, long-term oral anticoagulant therapy with warfarin at a target INR of 2.0 to 3.0 is recommended (*Class I; Level of Evidence A*).
2. For patients with nonvalvular AF, a CHA₂DS₂-VASC score of ≥ 2 , and acceptably low risk for hemorrhagic

complications, oral anticoagulants are recommended (*Class I*). Options include warfarin (INR, 2.0 to 3.0) (*Level of Evidence A*), dabigatran (*Level of Evidence B*), apixaban (*Level of Evidence B*), and rivaroxaban (*Level of Evidence B*). The selection of antithrombotic agent should be individualized on the basis of patient risk factors (particularly risk for intracranial hemorrhage), cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including the time that the INR is in therapeutic range for patients taking warfarin.

3. Active screening for AF in the primary care setting in patients >65 years of age by pulse assessment followed by ECG as indicated can be useful (*Class IIa; Level of Evidence B*).
4. For patients with nonvalvular AF and CHA₂DS₂-VASC score of 0, it is reasonable to omit antithrombotic therapy (*Class IIa; Level of Evidence B*).
5. For patients with nonvalvular AF, a CHA₂DS₂-VASC score of 1, and an acceptably low risk for hemorrhagic complication, no antithrombotic therapy, anticoagulant therapy, or aspirin therapy may be considered (*Class IIb; Level of Evidence C*). The selection of antithrombotic agent should be individualized on the basis of patient risk factors (particularly risk for intracranial hemorrhage), cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including the time that the INR is in the therapeutic range for patients taking warfarin.
6. Closure of the LAA may be considered for high-risk patients with AF who are deemed unsuitable for anticoagulation if performed at a center with low rates of periprocedural complications and the patient can tolerate the risk of at least 45 days of postprocedural anticoagulation (*Class IIb; Level of Evidence B*).

Other Cardiac Conditions: Recommendations

1. Anticoagulation is indicated in patients with mitral stenosis and a prior embolic event, even in sinus rhythm (*Class I; Level of Evidence B*).
2. Anticoagulation is indicated in patients with mitral stenosis and left atrial thrombus (*Class I; Level of Evidence B*).
3. Warfarin (target INR, 2.0–3.0) and low-dose aspirin are indicated after aortic valve replacement with bileaflet mechanical or current-generation, single-tilting-disk prostheses in patients with no risk factors* (*Class I; Level of Evidence B*); warfarin (target INR, 2.5–3.5) and low-dose aspirin are indicated in patients with mechanical aortic valve replacement and risk factors* (*Class I; Level of Evidence B*); and warfarin (target INR, 2.5–3.5) and low-dose aspirin are indicated after mitral valve replacement with any mechanical valve (*Class I; Level of Evidence B*).
4. Surgical excision is recommended for the treatment of atrial myxomas (*Class I; Level of Evidence C*).
5. Surgical intervention is recommended for symptomatic fibroelastomas and for fibroelastomas that are >1 cm or

*Risk factors include AF, previous thromboembolism, left ventricular dysfunction, and hypercoagulable condition.

appear mobile, even if asymptomatic (*Class I; Level of Evidence C*).

6. Aspirin is reasonable after aortic or mitral valve replacement with a bioprosthesis (*Class IIa; Level of Evidence B*).
7. It is reasonable to give warfarin to achieve an INR of 2.0 to 3.0 during the first 3 months after aortic or mitral valve replacement with a bioprosthesis (*Class IIa; Level of Evidence C*).
8. Anticoagulants or antiplatelet agents are reasonable for patients with heart failure who do not have AF or a previous thromboembolic event (*Class IIa; Level of Evidence A*).
9. Vitamin K antagonist therapy is reasonable for patients with STEMI and asymptomatic left ventricular mural thrombi (*Class IIa; Level of Evidence C*).
10. Anticoagulation may be considered for asymptomatic patients with severe mitral stenosis and left atrial dimension ≥ 55 mm by echocardiography (*Class IIb; Level of Evidence B*).
11. Anticoagulation may be considered for patients with severe mitral stenosis, an enlarged left atrium, and spontaneous contrast on echocardiography (*Class IIb; Level of Evidence C*).
12. Anticoagulant therapy may be considered for patients with STEMI and anterior apical akinesis or dyskinesis (*Class IIb; Level of Evidence C*).
13. Antithrombotic treatment and catheter-based closure are not recommended in patients with PFO for primary prevention of stroke (*Class III; Level of Evidence C*).

Asymptomatic Carotid Stenosis: Recommendations

1. Patients with asymptomatic carotid stenosis should be prescribed daily aspirin and a statin. Patients should also be screened for other treatable risk factors for stroke, and appropriate medical therapies and lifestyle changes should be instituted (*Class I; Level of Evidence C*).
2. In patients who are to undergo CEA, aspirin is recommended perioperatively and postoperatively unless contraindicated (*Class I; Level of Evidence C*).
3. It is reasonable to consider performing CEA in asymptomatic patients who have $>70\%$ stenosis of the internal carotid artery if the risk of perioperative stroke, MI, and death is low ($<3\%$). However, its effectiveness compared with contemporary best medical management alone is not well established (*Class IIa; Level of Evidence A*).
4. It is reasonable to repeat duplex ultrasonography annually by a qualified technologist in a certified laboratory to assess the progression or regression of disease and response to therapeutic interventions in patients with atherosclerotic stenosis $>50\%$ (*Class IIa; Level of Evidence C*).
5. Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum, 60% by angiography, 70% by validated Doppler ultrasound), but its effectiveness compared with medical therapy alone in this situation is not well established (*Class IIb; Level of Evidence B*).
6. In asymptomatic patients at high risk of complications for carotid revascularization by either CEA or CAS, the effectiveness of revascularization versus medical

therapy alone is not well established (*Class IIb; Level of Evidence B*).

7. Screening low-risk populations for asymptomatic carotid artery stenosis is not recommended (*Class III; Level of Evidence C*).

SCD: Recommendations

1. TCD screening for children with SCD is indicated starting at 2 years of age and continuing annually to 16 years of age (*Class I; Level of Evidence B*).
2. Transfusion therapy (target reduction of hemoglobin S, $<30\%$) is effective for reducing stroke risk in those children at elevated risk (*Class I; Level of Evidence B*).
3. Although the optimal screening interval has not been established, it is reasonable for younger children and those with borderline abnormal TCD velocities to be screened more frequently to detect the development of high-risk TCD indications for intervention (*Class IIa; Level of Evidence B*).
4. Pending further studies, continued transfusion, even in those whose TCD velocities revert to normal, is probably indicated (*Class IIa; Level of Evidence B*).
5. In children at high risk for stroke who are unable or unwilling to be treated with periodic red cell transfusion, it might be reasonable to consider hydroxyurea or bone marrow transplantation (*Class IIb; Level of Evidence B*).
6. MRI and MRA criteria for selection of children for primary stroke prevention with transfusion have not been established, and these tests are not recommended in place of TCD for this purpose (*Class III; Level of Evidence B*).

Migraine: Recommendations

1. Smoking cessation should be strongly recommended in women with migraine headaches with aura (*Class I; Level of Evidence B*).
2. Alternatives to OCS, especially those containing estrogen, might be considered in women with active migraine headaches with aura (*Class IIb; Level of Evidence B*).
3. Treatments to reduce migraine frequency might be reasonable to reduce the risk of stroke (*Class IIb; Level of Evidence C*).
4. Closure of PFO is not indicated for preventing stroke in patients with migraine (*Class III; Level of Evidence B*).

Metabolic Syndrome: Recommendations

1. Management of individual components of the metabolic syndrome is recommended, including lifestyle measures (ie, exercise, appropriate weight loss, proper diet) and pharmacotherapy (ie, medications for BP lowering, lipid lowering, glycemic control, and antiplatelet therapy), as endorsed in other sections of this guideline. (Refer to relevant sections for Class and Levels of Evidence for each recommendation.)

Alcohol Consumption: Recommendations

1. Reduction or elimination of alcohol consumption in heavy drinkers through established screening and counseling strategies as described in the 2004 US Preventive Services Task Force update is recommended⁷⁰³ (*Class I; Level of Evidence A*).
2. For individuals who choose to drink alcohol, consumption of ≤ 2 drinks per day for men and ≤ 1 drink per day for nonpregnant women might be reasonable^{704,705} (*Class IIb; Level of Evidence B*).

Drug Abuse: Recommendation

1. Referral to an appropriate therapeutic program is reasonable for patients who abuse drugs that have been associated with stroke, including cocaine, khat, and amphetamines (*Class IIa; Level of Evidence C*).

Sleep-Disordered Breathing: Recommendations

1. Because of its association with stroke risk, screening for sleep apnea through a detailed history, including structured questionnaires such as the Epworth Sleepiness Scale and Berlin Questionnaire, physical examination, and, if indicated, polysomnography may be considered (*Class IIb; Level of Evidence C*).
2. Treatment of sleep apnea to reduce the risk of stroke may be reasonable, although its effectiveness for primary prevention of stroke is unknown (*Class IIb; Level of Evidence C*).

Hyperhomocysteinemia: Recommendation

1. The use of the B complex vitamins, cobalamin (B_{12}), pyridoxine (B_6), and folic acid might be considered for the prevention of ischemic stroke in patients with hyperhomocysteinemia, but its effectiveness is not well established (*Class IIb; Level of Evidence B*).

Elevated Lp(a): Recommendations

1. The use of niacin, which lowers Lp(a), might be reasonable for the prevention of ischemic stroke in patients with high Lp(a), but its effectiveness is not well established (*Class IIb; Level of Evidence B*).
2. The clinical benefit of using Lp(a) in stroke risk prediction is not well established (*Class IIb; Level of Evidence B*).

Hypercoagulability: Recommendations

1. The usefulness of genetic screening to detect inherited hypercoagulable states for the prevention of first stroke is not well established (*Class IIb; Level of Evidence C*).
2. The usefulness of specific treatments for primary stroke prevention in asymptomatic patients with a hereditary or acquired thrombophilia is not well established (*Class IIb; Level of Evidence C*).

3. Low-dose aspirin (81 mg/d) is not indicated for primary stroke prevention in individuals who are persistently aPL positive (*Class III; Level of Evidence B*).

Inflammation and Infection: Recommendations

1. Patients with chronic inflammatory disease such as RA or SLE should be considered at increased risk of stroke (*Class I; Level of Evidence B*).
2. Annual influenza vaccination can be useful in lowering stroke risk in patients at risk of stroke (*Class IIa; Level of Evidence B*).
3. Measurement of inflammatory markers such as hs-CRP or lipoprotein-associated phospholipase A2 in patients without CVD may be considered to identify patients who may be at increased risk of stroke, although their usefulness in routine clinical practice is not well established (*Class IIb; Level of Evidence B*).
4. Treatment of patients with hs-CRP >2.0 mg/dL with a statin to decrease stroke risk might be considered (*Class IIb; Level of Evidence B*).
5. Treatment with antibiotics for chronic infections as a means to prevent stroke is not recommended (*Class III; Level of Evidence A*).

Antiplatelet Agents and Aspirin: Recommendations:

1. The use of aspirin for cardiovascular (including but not specific to stroke) prophylaxis is reasonable for people whose risk is sufficiently high (10-year risk $>10\%$) for the benefits to outweigh the risks associated with treatment. A cardiovascular risk calculator to assist in estimating 10-year risk can be found online at <http://my.americanheart.org/cvriskscalculator> (*Class IIa; Level of Evidence A*).
2. Aspirin (81 mg daily or 100 mg every other day) can be useful for the prevention of a first stroke among women, including those with diabetes mellitus, whose risk is sufficiently high for the benefits to outweigh the risks associated with treatment (*Class IIa; Level of Evidence B*).
3. Aspirin might be considered for the prevention of a first stroke in people with chronic kidney disease (ie, estimated glomerular filtration rate <45 mL/min/1.73 m²) (*Class IIb; Level of Evidence C*). This recommendation does not apply to severe kidney disease (stage 4 or 5; estimated glomerular filtration rate <30 mL/min/1.73 m²).
4. Cilostazol may be reasonable for the prevention of a first stroke in people with peripheral arterial disease (*Class IIb; Level of Evidence B*).
5. Aspirin is not useful for preventing a first stroke in low-risk individuals (*Class III; Level of Evidence A*).
6. Aspirin is not useful for preventing a first stroke in people with diabetes mellitus in the absence of other high-risk conditions (*Class III; Level of Evidence A*).
7. Aspirin is not useful for preventing a first stroke in people with diabetes mellitus and asymptomatic peripheral artery disease (defined as asymptomatic in the presence of an ankle brachial index ≤ 0.99) (*Class III; Level of Evidence B*).

Table 3. New and Revised Recommendations for 2014*

Section	2014 Recommendation	Description of Change from 2011
Assessing the risk of first stroke	The use of a risk assessment tool such as the AHA/ACC CV Risk Calculator (http://my.americanheart.org/cvriskscalculator) is reasonable because these tools can help identify individuals who could benefit from therapeutic interventions and who may not be treated on the basis of any single risk factor. These calculators are useful to alert clinicians and patients of possible risk, but basing treatment decisions on the results needs to be considered in the context of the overall risk profile of the patient (<i>Class IIa; Level of Evidence B</i>).	Reworded to add AHA/ACC CV Risk Calculator and link
Genetic factors	Treatment of Fabry disease with enzyme replacement therapy might be considered but has not been shown to reduce the risk of stroke, and its effectiveness is unknown (<i>Class IIb; Level of Evidence C</i>).	Slightly reworded; no change in class or level of evidence
	Screening for intracranial aneurysms in every carrier of autosomal-dominant polycystic kidney disease or Ehlers-Danlos type 4 mutations is not recommended (<i>Class III; Level of Evidence C</i>).	Previous statement was worded with less specificity, referring to “mendelian disorders associated with aneurysms”
	Pharmacogenetic dosing of vitamin K antagonists may be considered when therapy is initiated (<i>Class IIb; Level of Evidence C</i>).	Changed from Class III (is not recommended) to Class IIb (may be considered)
Physical inactivity	Healthy adults should perform at least moderate- to vigorous-intensity aerobic physical activity at least 40 min a day 3 to 4 d/wk (<i>Class I; Level of Evidence B</i>).	Changed wording to match new AHA lifestyle guideline
Dyslipidemia	In addition to therapeutic lifestyle changes, treatment with an HMG coenzyme-A reductase inhibitor (statin) medication is recommended for primary prevention of ischemic stroke in patients estimated to have a high 10-y risk for cardiovascular events as recommended in the 2013 “ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults” (<i>Class I; Level of Evidence A</i>).	Reworded to incorporate ACC/AHA guidelines (instead of NCEP); no change in class/LOE. Focusing on estimated cardiovascular risk as the determinant for initiating therapy is new.
	Niacin may be considered for patients with low high-density lipoprotein cholesterol or elevated lipoprotein(a), but its efficacy in preventing ischemic stroke in patients with these conditions is not established. Caution should be used with niacin because it increases the risk of myopathy (<i>Class IIb; Level of Evidence B</i>).	Changed from LOE C to LOE B; the risk of myopathy is highlighted
	Treatment with nonstatin lipid-lowering therapies such as fibric acid derivatives, bile acid sequestrants, niacin, and ezetimibe may be considered in patients who cannot tolerate statins, but their efficacy in preventing stroke is not established (<i>Class IIb; Level of Evidence C</i>).	Reworded from “other” to “nonstatin” (no change in class or LOE). Reference is no longer made to a low-density lipoprotein target for statin therapy because the decision to use moderate or intensive statin therapy depends on estimated risk of future cardiovascular events.
Diet and nutrition	A Mediterranean diet supplemented with nuts may be considered in lowering the risk of stroke (<i>Class IIb; Level of Evidence B</i>).	New recommendation
Hypertension	Regular blood pressure screening and appropriate treatment of patients with hypertension, including lifestyle modification and pharmacological therapy, are recommended (<i>Class I; Level of Evidence A</i>).	New recommendations
	Annual blood pressure screening for high blood pressure and health-promoting lifestyle modification are recommended for patients with prehypertension (systolic blood pressure of 120–139 mm Hg or diastolic blood pressure of 80–89 mm Hg) (<i>Class I; Level of Evidence A</i>).	
	Successful reduction of blood pressure is more important in reducing stroke risk than the choice of a specific agent, and treatment should be individualized on the basis of other patient characteristics and medication tolerance (<i>Class I; Level of Evidence A</i>).	New recommendation
	Self-measured blood pressure monitoring is recommended to improve blood pressure control (<i>Class I; Level of Evidence A</i>).	New recommendation
Obesity and body fat distribution	Among overweight (body mass index=25 to 29 kg/m ²) and obese (body mass index >30 kg/m ²) individuals, weight reduction is recommended for lowering blood pressure (<i>Class I; Level of Evidence A</i>).	Overweight and obesity have now been defined on the basis of body mass index

(Continued)

Table 3. Continued

Section	2014 Recommendation	Description of Change from 2011
Obesity and body fat distribution cont'd	Among overweight (body mass index=25 to 29 kg/m ²) and obese (body mass index >30 kg/m ²) individuals, weight reduction is recommended for reducing the risk of stroke (<i>Class I; Level of Evidence B</i>).	Overweight and obesity have now been defined on the basis of body mass index, and the recommendation has been upgraded from IIa to I
Diabetes mellitus	Control of blood pressure in accordance with an AHA/ACC/CDC advisory to a target of <140/90 mm Hg is recommended in patients with type 1 or type 2 diabetes mellitus (<i>Class I; Level of Evidence A</i>).	Reworded to reference AHA/ACC/CDC advisory
	The usefulness of aspirin for primary stroke prevention for patients with diabetes mellitus but low 10-y risk of cardiovascular disease is unclear (<i>Class IIb; Level of Evidence B</i>).	Deleted the phrase "however, administering aspirin may be reasonable"
Cigarette smoking	Counseling in combination with drug therapy using nicotine replacement, bupropion, or varenicline is recommended for active smokers to assist in quitting smoking (<i>Class I; Level of Evidence A</i>).	Reworded and LOE changed from B to A
	Community-wide or statewide bans on smoking in public spaces are reasonable for reducing the risk of stroke and myocardial infarction (<i>Class IIa; Level of Evidence B</i>).	New recommendation
Atrial fibrillation	For patients with valvular atrial fibrillation at high risk for stroke, defined as a CHA ₂ DS ₂ -VASc score of ≥2, and acceptably low risk for hemorrhagic complications, chronic oral anticoagulant therapy with warfarin at a target INR of 2.0 to 3.0 is recommended (<i>Class I; Level of Evidence A</i>).	New recommendation
	For patients with nonvalvular atrial fibrillation, a CHA ₂ DS ₂ -VASc score of ≥2, and acceptably low risk for hemorrhagic complications, oral anticoagulants are recommended (<i>Class I</i>). Options include warfarin (INR, 2.0 to 3.0) (<i>Level of Evidence A</i>), dabigatran (<i>Level of Evidence B</i>), apixaban (<i>Level of Evidence B</i>), and rivaroxaban (<i>Level of Evidence B</i>). The selection of antithrombotic agent should be individualized on the basis of patient risk factors (particularly risk for intracranial hemorrhage), cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including time INR is in therapeutic range for patients taking warfarin.	New recommendation
	For patients with nonvalvular atrial fibrillation and CHA ₂ DS ₂ -VASc score of 0, it is reasonable to omit antithrombotic therapy (<i>Class IIa; Level of Evidence B</i>).	New recommendation
	For patients with nonvalvular atrial fibrillation, a CHA ₂ DS ₂ -VASc score of 1, and acceptably low risk for hemorrhagic complication, no antithrombotic therapy, anticoagulant therapy, or aspirin therapy may be considered (<i>Class IIb; Level of Evidence C</i>). The selection of antithrombotic agent should be individualized on the basis of patient risk factors (particularly risk for intracranial hemorrhage), cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including time INR is in therapeutic range for patients taking warfarin.	New recommendation
	Closure of the left atrial appendage may be considered for high-risk patients with atrial fibrillation who are deemed unsuitable for anticoagulation if performed at a center with low rates of periprocedural complications and the patient can tolerate the risk of at least 45 d of postprocedural anticoagulation (<i>Class IIb; Level of Evidence B</i>).	New recommendation
Other cardiac conditions	Anticoagulation is indicated in patients with mitral stenosis and a prior embolic event, even in sinus rhythm (<i>Class I; Level of Evidence B</i>).	New recommendation
	Anticoagulation is indicated in patients with mitral stenosis and left atrial thrombus (<i>Class I; Level of Evidence B</i>).	New recommendation
	Warfarin (target INR, 2.0–3.0) and low-dose aspirin are indicated after aortic valve replacement with bileaflet mechanical or current-generation, single-tilting-disk prostheses in patients with no risk factors* (<i>Class I; Level of Evidence B</i>); warfarin (target INR, 2.5–3.5) and low-dose aspirin are indicated in patients with mechanical aortic valve replacement and risk factors* (<i>Class I; Level of Evidence B</i>); and warfarin (target INR, 2.5–3.5) and low-dose aspirin are indicated after mitral valve replacement with any mechanical valve (<i>Class I; Level of Evidence B</i>).	New recommendations
	Surgical excision is recommended for treatment of atrial myxomas (<i>Class I; Level of Evidence C</i>).	New recommendation

(Continued)

Table 3. Continued

Section	2014 Recommendation	Description of Change from 2011
Other cardiac conditions cont'd	Surgical intervention is recommended for symptomatic fibroelastomas and for fibroelastomas that are >1 cm or appear mobile, even if asymptomatic (<i>Class I; Level of Evidence C</i>).	New recommendation
	Aspirin is reasonable after aortic or mitral valve replacement with a bioprosthesis (<i>Class IIa; Level of Evidence C</i>).	New recommendation
	It is reasonable to give warfarin to achieve an INR of 2.0–3.0 during the first 3 mo after aortic or mitral valve replacement with a bioprosthesis (<i>Class IIa; Level of Evidence C</i>).	New recommendation
	Anticoagulants or antiplatelet agents are reasonable for patients with heart failure who do not have atrial fibrillation or a previous thromboembolic event (<i>Class IIa; Level of Evidence A</i>).	New recommendation
	Vitamin K antagonist therapy is reasonable for patients with ST-segment–elevation myocardial infarction and asymptomatic left ventricular mural thrombi (<i>Class IIa; Level of Evidence C</i>).	The level of evidence has been downgraded from A to C, but the recommendation grade is the same
	Anticoagulation may be considered for asymptomatic patients with severe mitral stenosis and left atrial dimension ≥ 55 mm by echocardiography (<i>Class IIb; Level of Evidence B</i>).	New recommendation
	Anticoagulation may be considered for patients with severe mitral stenosis, an enlarged left atrium, and spontaneous contrast on echocardiography (<i>Class IIb; Level of Evidence C</i>).	New recommendation
	Anticoagulant therapy may be considered for patients with ST-segment–elevation myocardial infarction and anterior apical akinesis or dyskinesis (<i>Class IIb; Level of Evidence C</i>).	New recommendation
	Antithrombotic treatment and catheter-based closure are not recommended in patients with patent foramen ovale for primary prevention of stroke (<i>Class III; Level of Evidence C</i>).	New recommendation
Asymptomatic carotid stenosis	Patients with asymptomatic carotid stenosis should be prescribed daily aspirin and a statin. Patients should also be screened for other treatable risk factors for stroke, and appropriate medical therapies and lifestyle changes should be instituted (<i>Class I; Level of Evidence C</i>).	New recommendation. The use of aspirin and statin therapy was implied but not explicitly stated except in the perioperative and postoperative context in the prior guidelines.
	It is reasonable to consider performing carotid endarterectomy in asymptomatic patients who have >70% stenosis of the internal carotid artery if the risk of perioperative stroke, myocardial infarction, and death is low (<3%). However, its effectiveness compared with contemporary best medical management alone is not well established (<i>Class IIa; Level of Evidence A</i>).	New recommendation
	It is reasonable to repeat duplex ultrasonography annually by a qualified technologist in a certified laboratory to assess the progression or regression of disease and response to therapeutic interventions in patients with atherosclerotic stenosis >50% (<i>Class IIa; Level of Evidence C</i>).	New recommendation
	Prophylactic carotid angioplasty and stenting might be considered in highly selected patients with asymptomatic carotid stenosis (minimum, 60% by angiography, 70% by validated Doppler ultrasound), but its effectiveness compared with medical therapy alone in this situation is not well established (<i>Class IIb; Level of Evidence B</i>).	New recommendation
	In asymptomatic patients at high risk of complications for carotid revascularization by either carotid endarterectomy or carotid angioplasty and stenting, the effectiveness of revascularization versus medical therapy alone is not well established (<i>Class IIb; Level of Evidence B</i>).	New recommendation
Sickle cell disease	Transcranial Doppler screening for children with sickle cell disease is indicated starting at 2 y of age and continuing annually to 16 y of age (<i>Class I; Level of Evidence B</i>).	Slightly reworded to include up to 16 y (no change in class or LOE)
	In children at high risk for stroke who are unable or unwilling to be treated with periodic red cell transfusion, it might be reasonable to consider hydroxyurea or bone marrow transplantation (<i>Class IIb; Level of Evidence B</i>).	Changed from LOE C to LOE B
Migraine	Smoking cessation should be strongly recommended in women with migraine headaches with aura (<i>Class I; Level of Evidence B</i>).	New recommendation
	Alternatives to oral contraceptives, especially those containing estrogen, might be considered in women with active migraine headaches with aura (<i>Class IIb; Level of Evidence B</i>).	New recommendation

(Continued)

Table 3. Continued

Section	2014 Recommendation	Description of Change from 2011
Migraine cont'd	Closure of patent foramen ovale is not indicated for preventing stroke in patients with migraine (<i>Class III; Level of Evidence B</i>).	New recommendation
Drug abuse	Referral to an appropriate therapeutic program is reasonable for patients who abuse drugs that have been associated with stroke, including cocaine, khat, and amphetamines (<i>Class IIa; Level of Evidence C</i>).	Wording slightly revised to specifically list drugs associated with stroke
Sleep-disordered breathing	Because of its association with stroke risk, screening for sleep apnea through a detailed history, including structured questionnaires such as the Epworth Sleepiness Scale and Berlin Questionnaire, physical examination, and, if indicated, polysomnography may be considered (<i>Class IIb; Level of Evidence C</i>).	Wording slightly revised to include polysomnography and use of specific questionnaires. Recommendation class and LOE have been downgraded.
Elevated lipoprotein(a)	The clinical benefit of using lipoprotein(a) in stroke risk prediction is not well established (<i>Class IIb; Level of Evidence B</i>).	New recommendation
Inflammation and infection	Treatment of patients with high-sensitivity C-reactive protein >2.0 mg/dL with a statin to decrease stroke risk might be considered (<i>Class IIb; Level of Evidence B</i>).	The revised recommendation now defines elevated high-sensitivity C-reactive protein as >2.0 mg/dL in the context of considering statin initiation
Antiplatelet agents and aspirin	The use of aspirin for cardiovascular (including but not specific to stroke) prophylaxis is reasonable for people whose risk is sufficiently high (10-y risk >10%) for the benefits to outweigh the risks associated with treatment. A cardiovascular risk calculator to assist in estimating 10-y risk can be found online at http://my.americanheart.org/cvriskscalculator (<i>Class IIa; Level of Evidence A</i>).	Reworded to include cardiovascular risk calculator and link; changed from Class I to IIa
	Aspirin might be considered for the prevention of a first stroke in people with chronic kidney disease (ie, estimated glomerular filtration rate <45 mL·min ⁻¹ ·1.73 m ⁻²) (<i>Class IIb; Level of Evidence C</i>). This recommendation does not apply to severe kidney disease (stage 4 or 5; estimated glomerular filtration rate <30 mL·min ⁻¹ ·1.73 m ⁻²).	New recommendation
	Cilostazol may be reasonable for the prevention of a first stroke in people with peripheral arterial disease (<i>Class IIb; Level of Evidence B</i>).	New recommendation
	As a result of a lack of relevant clinical trials, antiplatelet regimens other than aspirin and cilostazol are not recommended for the prevention of a first stroke (<i>Class III; Level of Evidence C</i>).	New recommendation

ACC indicates American College of Cardiology; AHA, American Heart Association; CDC, Centers for Disease Control and Prevention; CV, cardiovascular; INR, international normalized ratio; LOE, level of evidence; and NCEP, National Cholesterol Education Program.

*This table does not include recommendations that have been removed.

8. The use of aspirin for other specific situations (eg, AF, carotid artery stenosis) is discussed in the relevant sections of this statement.
9. As a result of a lack of relevant clinical trials, antiplatelet regimens other than aspirin and cilostazol are not recommended for the prevention of a first stroke (*Class III; Level of Evidence C*).

5. The effectiveness of screening, brief intervention, and referral for treatment of diabetes mellitus and lifestyle stroke risk factors (obesity, alcohol/substance abuse, sedentary lifestyle) in the ED setting is not established (*Class IIb; Level of Evidence C*).

Primary Prevention in the ED: Recommendations

1. ED-based smoking cessation programs and interventions are recommended (*Class I; Level of Evidence B*).
2. Identification of AF and evaluation for anticoagulation in the ED are recommended (*Class I; Level of Evidence B*).
3. ED population screening for hypertension is reasonable (*Class IIa; Level of Evidence C*).
4. When a patient is identified as having a drug or alcohol abuse problem, ED referral to an appropriate therapeutic program is reasonable (*Class IIa; Level of Evidence C*).

Preventive Health Services: Recommendation

1. It is reasonable to implement programs to systematically identify and treat risk factors in all patients at risk for stroke (*Class IIa; Level of Evidence A*).

Acknowledgments

We thank medical librarians Ann Farrell at Mayo Clinic Rochester and Tara Brigham at Mayo Clinic Florida for assistance with a systematic review of the medical literature.

References

References are available in the full text of this guideline: <http://stroke.ahajournals.org/cgi/reprint/STR.0000000000000046>.